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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,975	01/18/2002	Limin Li	STAN-216	5176
23552 7590 06/26/2007 MERCHANT & GOULD PC P.O. BOX 2903 MINNEAPOLIS, MN 55402-0903			EXAMINER FETTEROLF, BRANDON J	
			ART UNIT 1642	PAPER NUMBER
			MAIL DATE 06/26/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/053,975	LI ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-16,22-25,31,32 and 37-50 is/are pending in the application.
- 4a) Of the above claim(s) 7-16,22-25,31,32,37-42,44 and 45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-6,43 and 46-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/18/2007 has been entered.

Claims 1, 4-16, 22-25, 31-32 and 37-50 are pending.

Claims 7-16, 22-25, 31-32, 37-42 and 44-45 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 4-6, 43 and 46-50 are currently pending.

Claim Objections

Claims 47-49 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claims 47-49 each limit the ubiquitination-regulating domain recited in claim 46 to comprising amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1. However, independent claim 46 already sets forth that the ubiquitination domain consists of amino acid residues 1 to 250 of SEQ ID NO: 1. As such, it is unclear how the "comprising" language recited in claims 47-49 which is "open-ended" further limits the "consisting" language recited in independent claim 46.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 46-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

New claims 46 and 50 are specifically drawn to an isolated antibody that binds to a ubiquitination-regulating domain or a functional fragment thereof, wherein said domain consists of amino acids 1-250 and a pharmaceutical composition comprising said antibody of claim 46. New claims 47-49 depend from claim 46 and further limit said ubiquitination regulating domain to consist of amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1. However, the specification and claims, as originally filed, do not appear to lend support for the limitation that the ubiquitination-regulating domain consists of amino acid residues 1-250, 50-140, 1-140 or 140-250. For example, Applicants submitted that support for new claims 46-50 can be found on page 2, line 20 to page 3, line 9 of the specification as filed and in original claims 1, 4-6 and 43. However, the specification on page 2, line 20 to page 3, line 9 and original claims 1, 4-6 and 43 only appear to lend support to a ubiquitination-regulating domain comprising amino acid residues 1-250, 50-140, 1-140 and 140-250 of SEQ ID NO: 1 which is different from a ubiquitination-regulating domain consisting of amino acid residues 1-250, 50-140, 1-140 and 140-250 of SEQ ID NO: 1 (*see* MPEP, 2111.03). Applicant is invited to point to clear support or specific examples of the claimed limitation in the specification as-filed or remove such amendatory language in response to this office action.

Note: In order to expedite prosecution, the Examiner would like to respond to Applicants arguments pertaining to the previous rejection as they relate to the current rejection. In response to the previous rejection, Applicants assert that it is unarguable that reading the specification reasonably conveys to one of skill in the art the Applicants' recognition that ubiquitination region can be found in the first 250 amino acids, and that an antibody drawn thereto may be therapeutically effective. Thus, Applicants assert that the language in question has been amended, as unnecessary to define over the prior art, as noted above.

These arguments have been carefully considered, but are not found persuasive.

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In the instant case, the Examiner recognizes that while Applicants assert that the specification reasonably conveys to one of skill in the art Applicants recognition that ubiquitination region can be found in the first 250 amino acids, Applicants have not provided any clear support or pointed to any specific examples of the claimed limitation in the specification. As noted above, the specification as a whole, see for example, page 2, line 20 to page 3, line 9 and original claims 1, 4-6 and 43, only appear to lend support to a ubiquitination-regulating domain comprising amino acid residues 1-250, 50-140, 1-140 and 140-250 of SEQ ID NO: 1 which is different from a ubiquitination-regulating domain consisting of amino acid residues 1-250, 50-140, 1-140 and 140-250 of SEQ ID NO: 1 (*see* MPEP, 2111.03).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-6, 43 and 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999) as evidenced by Pornillos et al. (The EMBO Journal 2002; 21: 2397-2406).

Li. et al. teach antibodies which have been raised to normal or mutated forms of TSG101 (column 8, line 59-63). Specifically, the patent teaches antibodies that specifically recognize the coiled domain, leucine zipper and proline rich domains of TSG101 (column 8, lines 64 to column 9, line 4). With regards to TSG101, Li et al. provide both the mouse TSG101 and the human homolog (column 3, lines 26-38, see below, human homolog). Although the reference does not specifically teach that the antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ ID NO: 1, the claimed limitation does not to appear to result in a manipulative difference between the prior art because as taught by the specification (page 10, *Overview*) and as evidenced by Pornillos et al., the proline rich domain (referred to as PRD) and at least a portion of the coiled domain (referred to as COIL) lies within amino acid residues 1-250 of SEQ ID NO: 1 (page 2398, Figure 1A). Thus, the claimed antibody

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appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Lastly, the transitional term “comprising”, which is synonymous with “including,” “containing,” or “characterized by,” is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. As such, the limitation that the antibody binds to an epitope in the ubiquitination regulating domain of TSG101, wherein the ubiquitination regulating domain “comprises” amino acid residues 50-140 or 1-140 of SEQ ID NO: 1, does not appear to result in difference between the antibodies taught by Li et al. which specifically binds to the proline rich domain of TSG101 for the reasons set forth above.

Patent No. 5891668

APPLICANT: LI, Limin

APPLICANT: COHEN, Stanley N

US-08-670-274B-4

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Query Match          97.8%;   Score 2002;   DB 2;   Length 380;
Best Local Similarity 100.0%;   Pred. No. 3e-155;
Matches 380;   Conservative 0;   Mismatches 0;   Indels 0;   Gaps
0;

Qy      11  MVSKYKYRDLTVRETVNVITLYKDLKPVLD SYVFNDGSSRELMNLTGTIPV PYRGNTYNI 70
      |||
Db      1  MVSKYKYRDLTVRETVNVITLYKDLKPVLD SYVFNDGSSRELMNLTGTIPV PYRGNTYNI 60

Qy      71  PICLWLLDTPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV 130
      |||
Db      61  PICLWLLDTPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV 120

Qy     131  MIVVFGDEPPVFSRPISASYPYQATGPPNTSYMPGMPGGISPYPSPGYPPNPSGYPGCPY 190
      |||
Db     121  MIVVFGDEPPVFSRPISASYPYQATGPPNTSYMPGMPGGISPYPSPGYPPNPSGYPGCPY 180

Qy     191  PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISED TIRASLISAVSDKLRWRMKEEMDRAQ 250
      |||
Db     181  PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISED TIRASLISAVSDKLRWRMKEEMDRAQ 240

Qy     251  AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE 310
      |||
Db     241  AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE 300

Qy     311  NNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ 370

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Db      301  |||||||||||||||||||||||||||||||||||||||||||||||||||||||| 360
          NNDIDEVVIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ
Qy      371  FQLRALMQKARKTAGLSDLY 390
          ||||||||||||||||
Db      361  FQLRALMQKARKTAGLSDLY 380
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Note: In order to expedite prosecution, the Examiner would like to respond to Applicants arguments. In response to this rejection, Applicants assert that all of the claims are directed to antibodies that are particularly characterized not only in that they bond to a polypeptide that comprises ubiquitination-regulating region of TSG101, but moreover, they specifically bind to an epitope in that region, in the first 250 amino acid of SEQ ID NO: 1. As such, Applicants assert that, as acknowledged by the Office Action, Li et al. neither recognizes the presence of an ubiquitination-regulating domain in TSG101, nor suggest directing an antibody to an epitope that is found within that region, within the first 250 amino acids. Applicants further assert that it is insufficient, to shoulder the burden of potential inherency, to point to the fact that Applicants' antibodies and the prior art are directed to the same protein, wherein Applicants' claims require that the antibody bind specifically to an epitope in a region of that protein which is not as recognized as of importance, or suggested, in the prior art.

These arguments have been carefully considered, but are not found persuasive.

First, with respect to Applicants amendments, the Examiner acknowledges that Applicants have amended the claims to characterize the claimed antibody by binding specificity. However, the Examiner recognizes that Li et al. clearly teaches antibodies which specifically bind to the coiled domain and/or proline rich domain of TSG101. Thus, as stated above, although the reference does not specifically teach that the antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ ID NO: 1, the claimed limitation does not appear to result in a manipulative difference between the prior art because as evidenced by Pornillos et al., the proline rich domain (referred to as PRD) and at least a portion of the coiled domain (referred to as COIL) lies within amino acid residues 1-250 of SEQ ID NO: 1 (page 2398, Figure 1A). As such, the claimed antibodies appear to be the same as the prior art.

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Claims 1, 4-6, 43 and 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999, *of record*):

Brie *et al.* teach a purified protein having an amino acid sequence having 100% identity to the amino acid sequence set forth in SEQ ID NO: 1 (Figures 1A-1B, *see below*). The patent further teaches antibodies including, but not limited to, polyclonal, monoclonal and chimeric which bind specifically to the polypeptide (column 17, line 15 to column 18, line 16). Furthermore, Brie et al. disclose that the antibodies can be used as a pharmaceutical agent for the prevention and or treatment of disease associated with expression of the polypeptide (column 16, lines 56-60). Although the reference does not specifically teach that the antibody binds to a polypeptide comprising a ubiquitination-regulating domain, the claims are drawn to the product *per se* and inherently, such an antibody would bind to a polypeptide comprising a ubiquitination-regulating domain. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

OS Homo sapiens.
PN US5892016-A.
PD 06-APR-1999.
PF 23-JAN-1997; 97US-00786999.
PR 23-JAN-1997; 97US-00786999.
PA (INCY-) INCYTE PHARM.
PI Brie SL, Góli SK;
SQ Sequence 390 AA;

Query Match 100.0%; Score 2047; DB 2; Length 390;
Best Local Similarity 100.0%; Pred. No. 6.7e-149;
Matches 390; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MAVSESQLKKMVSKYKYRDLTVRETVNVITLYKDLKPVLD SYVFNDGSSRELMNLTGTIP	60
Db	1	MAVSESQLKKMVSKYKYRDLTVRETVNVITLYKDLKPVLD SYVFNDGSSRELMNLTGTIP	60
Qy	61	VPYRGNTYNIPICLWLLDTPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHP	120
Db	61	VPYRGNTYNIPICLWLLDTPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHP	120

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Qy      121 QSDLLGLIQVMIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPP 180
        |||
Db      121 QSDLLGLIQVMIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPP 180

Qy      181 NPSGYPGCPYPPGGYPATTSSQYPSQPPVTTVGPSRDGTISED TIRASLISAVSDKLRW 240
        |||
Db      181 NPSGYPGCPYPPGGYPATTSSQYPSQPPVTTVGPSRDGTISED TIRASLISAVSDKLRW 240

Qy      241 RMKEEMDRAQAELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSS 300
        |||
Db      241 RMKEEMDRAQAELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSS 300

Qy      301 ALEKMENQSENNDIDEV I IPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFL 360
        |||
Db      301 ALEKMENQSENNDIDEV I IPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFL 360

Qy      361 KHVRLLSRKQFQLRALMQKARKTAGLSLDY 390
        |||
Db      361 KHVRLLSRKQFQLRALMQKARKTAGLSLDY 390

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Note: In order to expedite prosecution, the Examiner would like to respond to Applicants arguments. In response to this rejection, Applicants assert that all of the claims are directed to antibodies that are particularly characterized not only in that they bond to a polypeptide that comprises ubiquitination-regulating region of TSG101, but moreover, they specifically bind to an epitope in that region, in the first 250 amino acid of SEQ ID NO: 1. As such, Applicants assert that, as acknowledged by the Office Action, Brie et al. neither acknowledges the presence of an ubiquitination-regulating domain in TSG101, nor suggest that an epitope in the first 250 amino acids in that protein would be a beneficial binding site for an antibody. Typically, Applicants assert that in order to generate an antibody which binds preferentially (specifically) to an epitope in a particular region, an antibody would have to be raised against a template that reflects at least a portion of that region.

These arguments have been carefully considered, but are not found persuasive.

First, with respect to Applicants amendments, the Examiner acknowledges that Applicants have amended the claims to characterize the claimed antibody by binding specificity. However, the Examiner recognizes that the claims do not appear to recite that the antibodies are monoclonal. As such, the claims encompass polyclonal antibodies which are clearly taught by Brie et al and further, the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements

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or method steps. See, e.g., *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter*, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). In the instant case, it is clear that the instant ubiquitination regulating domain comprises amino acid residues 50-140 of SEQ ID NO: 1, 1-140 of SEQ ID NO: 1, or 140-250 of SEQ ID NO: 1. However, there does not appear to be a patentable difference between antibodies which bind to a polypeptide that is 100% identical (see sequence comparison) to a polypeptide comprising the amino acid sequence recited in SEQ ID NO: 1, wherein the ubiquitination-regulating domain comprises amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1 because the claims do not appear to limit and/or specifically define what the ubiquitination-regulating domain consists of. Lastly, with regards to Applicants assertions that Brie et al. did not recognize that in epitope in the first 250 amino acids of TSG101 would be a beneficial binding site for an antibody, the Examiner recognizes that mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

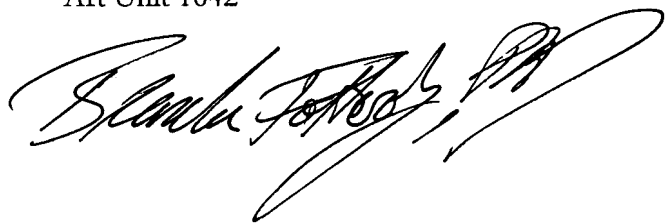
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF

A handwritten signature in black ink, appearing to read "Brandon J Fetterolf, PhD", with a large, stylized flourish extending from the end of the signature.